

INTERNATIONAL SEARCH REPORT

International Application No
PCT/DK2005/000222

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/424 A61P25/20 A61P11/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data, BIOSIS, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, A	WO 2005/023820 A (H. LUNDBECK A/S; PETERSEN, HANS; BECH SOMMER, MICHAEL; DANCER, ROBERT) 17 March 2005 (2005-03-17)	
X	WO 00/51590 A (THE BOARD OF TRUSTEES OF THE UNIVERSITY OF ILLINOIS; RADULOVACKI, MIOD) 8 September 2000 (2000-09-08) claims 15-18 page 6, paragraph 2 - paragraph 3	1-6, 9-19, 21-24
Y	WO 97/02813 A (MAX-PLANCK-GESELLSCHAFT ZUR FOERDERUNG DER WISSENSC) 30 January 1997 (1997-01-30) claims 1,8,12-14	1-24
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

22 July 2005

Date of mailing of the international search report

29/07/2005

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer


Bonzano, C

INTERNATIONAL SEARCH REPORT

International Application No
PCT/DK2005/000222

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>BEULLENS J: "Sleep disorders in older people, in particular sleep apnea syndrome: Are these a cause of sleeplessness?"</p> <p>TIJDSCHRIFT VOOR GERONTOLOGIE EN GERIATRIE 1999 NETHERLANDS, vol. 30, no. 6, 1999, pages 256-263, XP008050219</p> <p>ISSN: 0167-9228</p> <p>page 256, column 1, paragraph 2 - column 2, paragraph 1</p>	1-24
Y	<p>DUTSCHMANN M ET AL: "NMDA AND GABAA RECEPTORS IN THE RAT KOELLIKER-FUSE AREA CONTROL CARDIORESPIRATORY RESPONSES EVOKED BY TRIGEMINAL ETHMOIDAL NERVE STIMULATION" JOURNAL OF PHYSIOLOGY, vol. 510, no. 3, August 1998 (1998-08), pages 793-804, XP000922770</p> <p>ISSN: 0022-3751</p> <p>page 796, column 2</p> <p>page 798, column 1, paragraph 2 - column 2, paragraph 1</p>	1-24
A	<p>LIU X ET AL: "Suppression of genioglossus muscle tone and activity during reflex hypercapnic stimulation by GABAa mechanisms at the hypoglossal motor nucleus in vivo" NEUROSCIENCE, NEW YORK, NY, US, vol. 116, no. 1, 15 January 2003 (2003-01-15), pages 249-259, XP004631781</p> <p>ISSN: 0306-4522</p> <p>figure 3</p> <p>page 251, column 2, paragraph 5</p> <p>page 249, column 2, paragraph 1 - paragraph 2</p>	
A	<p>GATTI P J ET AL: "Cardiorespiratory effects produced by injecting drugs that affect GABA receptors into nuclei associated with the ventral surface of the medulla" NEUROPHARMACOLOGY 1987 UNITED KINGDOM, vol. 26, no. 5, 1987, pages 423-431, XP008050212</p> <p>page 430, column 1, paragraph 5 - column 2, paragraph 2</p>	
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INTERNATIONAL SEARCH REPORT

Inter  Application No
PCT/DK2005/000222

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	TAVEIRA DA SILVA A M ET AL: "RESPIRATORY DEPRESSANT EFFECTS OF GABA ALPHA AND BETA-RECEPTOR AGONISTS IN THE CAT" JOURNAL OF APPLIED PHYSIOLOGY, vol. 62, no. 6, 1987, pages 2264-2272, XP008050216 ISSN: 8750-7587 page 2270, column 1, paragraph 1 -----	
A	DARNALL ROBERT A ET AL: "The effects of a GABAA agonist in the rostral ventral medulla on sleep and breathing in newborn piglets" SLEEP (ROCHESTER), vol. 24, no. 5, 1 August 2001 (2001-08-01), pages 514-527, XP008050217 ISSN: 0161-8105 page 525, column 2, paragraph 2 -----	

INTERNATIONAL SEARCH REPORT

International application No.
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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 23,24 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/DK2005/000222

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2005023820	A	17-03-2005	WO 2005023820 A1	17-03-2005
WO 0051590	A	08-09-2000	WO 0051590 A2	08-09-2000
			US 2003236228 A1	25-12-2003
			US 6555564 B1	29-04-2003
WO 9702813	A	30-01-1997	DE 19525598 A1	16-01-1997
			AT 207349 T	15-11-2001
			AT 207352 T	15-11-2001
			AT 207356 T	15-11-2001
			AU 723954 B2	07-09-2000
			AU 6613796 A	10-02-1997
			CA 2226582 A1	30-01-1997
			DE 69616333 D1	29-11-2001
			DE 69616333 T2	04-07-2002
			DE 69616375 D1	29-11-2001
			DE 69616375 T2	11-07-2002
			DE 69616376 D1	29-11-2001
			DE 69616376 T2	27-06-2002
			DK 840601 T3	18-02-2002
			DK 867178 T3	18-02-2002
			DK 867184 T3	18-02-2002
			WO 9702813 A1	30-01-1997
			EP 0840601 A1	13-05-1998
			EP 0867178 A1	30-09-1998
			EP 0867184 A1	30-09-1998
			ES 2165990 T3	01-04-2002
			ES 2166110 T3	01-04-2002
			ES 2166111 T3	01-04-2002
			JP 11509194 T	17-08-1999
			JP 2005047925 A	24-02-2005
			PT 840601 T	29-04-2002
			PT 867178 T	29-04-2002
			PT 867184 T	29-04-2002
			US 5929065 A	27-07-1999

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 480-WO-PCT	FOR FURTHER ACTION		See item 4 below
International application No. PCT/DK2005/000222	International filing date (<i>day/month/year</i>) 31 March 2005 (31.03.2005)	Priority date (<i>day/month/year</i>) 02 April 2004 (02.04.2004)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant H. LUNDBECK A/S			

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).																								
2.	This REPORT consists of a total of 7 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.																								
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 30%;">Box No. I</td> <td style="width: 60%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<input type="checkbox"/>	Box No. VII	Certain defects in the international application																							
<input type="checkbox"/>	Box No. VIII	Certain observations on the international application																							
4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																								

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 2px;">Date of issuance of this report 04 October 2006 (04.10.2006)</td> </tr> <tr> <td style="padding: 2px;">Authorized officer <div style="text-align: center; font-weight: bold;">Simin Baharlou</div></td> </tr> <tr> <td style="padding: 2px;">e-mail: pt09@wipo.int</td> </tr> </table>	Date of issuance of this report 04 October 2006 (04.10.2006)	Authorized officer <div style="text-align: center; font-weight: bold;">Simin Baharlou</div>	e-mail: pt09@wipo.int
Date of issuance of this report 04 October 2006 (04.10.2006)				
Authorized officer <div style="text-align: center; font-weight: bold;">Simin Baharlou</div>				
e-mail: pt09@wipo.int				

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 27 JUL 2005

PCT

INT. D.

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/DK2005/000222

International filing date (day/month/year)
31.03.2005

Priority date (day/month/year)
02.04.2004

International Patent Classification (IPC) or both national classification and IPC
A61K31/424, A61P25/20, A61P11/00

Applicant
H. LUNDBECK AS

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Fax: +31 70 340 - 3016

Authorized Officer

Bonzano, C

Telephone No. +31 70 340-2202



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/DK2005/000222

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/DK2005/000222

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 23,24 with regard to industrial applicability

because:

- ☒ the said international application, or the said claims Nos. 23,24 with regard to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/DK2005/000222

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	7,8,20
	No: Claims	1-6,9-19,21-24
Inventive step (IS)	Yes: Claims	-
	No: Claims	1-24
Industrial applicability (IA)	Yes: Claims	1-22
	No: Claims	23,24 (see separate sheet)

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The subject matter of claims 23,24 concerns a method of treatment of the human/animal body which is considered by this Authority to be covered by the provisions of Rule 67.1 (IV) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of this claim (Article 34(4) (a)(I)PCT).

Re Item V

2. Reference is made to the following documents:

D1 : WO 00/51590 A (THE BOARD OF TRUSTEES OF THE UNIVERSITY OF ILLINOIS; RADULOVACKI, MIOD) 8 September 2000 (2000-09-08)

D2 : WO 97/02813 A (MAX-PLANCK-GESELLSCHAFT ZUR FOERDERUNG DER WISSENSC) 30 January 1997 (1997-01-30)

D3 : DUTSCHMANN M ET AL: "NMDA AND GABAA RECEPTORS IN THE RAT KOELLIKER-FUSE AREA CONTROL CARDIORESPIRATORY RESPONSES EVOKED BY TRIGEMINAL ETHMOIDAL NERVE STIMULATION" JOURNAL OF PHYSIOLOGY, vol. 510, no. 3, August 1998 (1998-08), pages 793-804, XP000922770 ISSN: 0022-3751

D4: BEULLENS J: "Sleep disorders in older people, in particular sleep apnea syndrome: Are these a cause of sleeplessness?" TIJDSCHRIFT VOOR GERONTOLOGIE EN GERIATRIE 1999 NETHERLANDS, vol. 30, no. 6, 1999, pages 256-263, XP008050219 ISSN: 0167-9228

3. For the assessment of the present claims 23,24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Novelty

4. The present application does not meet the criteria of Article 33(1) PCT, because the

subject-matter of claims 1-6,9-19,21-24 is not new in the sense of Article 33(2) PCT. Document D1 discloses a method of preventing or ameliorating sleep-related breathing disorders, in particular sleep apnea related breathing disorder, comprising administering to a patient in need thereof an effective amount of GABA receptor agonist, namely THIP (other name for gaboxadol). The subject-matter of claims 1-6,9-19,21-24 is therefore not new over D1 (Article 33(2) PCT).

Inventive step

5. The present application does not meet the criteria of Article 33(1) PCT, because the subject matter of claims 1-6,9-19,21-24, as far as novel, and 7,8,20 does not involve an inventive step in the sense of Article 33(3) PCT.

According to D4, among the most important sleep disorders is sleep apnea syndrome. The subject-matter of claims 1-24 differs from the disclosure of D4 in that sleep apnea syndrome is treated with the compound gaboxadol.

The problem to be solved by the present invention may therefore be regarded as finding an alternative treatment for sleep apnea syndrome.

Document D2 describes the GABA_A agonists muscimol and the present claimed compound THIP as having very advantageous effects on sleep: a method for treating a sleep disorder is disclosed, comprising administering a hypnotically effective amount of THIP, (other name for gaboxadol), wherein said sleep disorder is difficulty in falling asleep, frequent nocturnal arousal, wherein the amount of THIP administered is 5 to 50 mg per day.

It would be obvious for the man skilled in the art to use gaboxadol for treating sleep apnea, knowing that this compound is useful for treating sleep disorders in general and knowing that sleep apnea is one of the commonest sleep disorders.

Moreover, D3 discloses that the GABA_A antagonist bicuculline induces suppression of breathing and apnea during sleep. This teaching would strengthen the motivation of the man skilled in the art to try to use instead of a GABA_A antagonist a GABA agonist, such as gaboxadol, for treating the symptoms of apnea and stimulate breathing during sleep (Article 33(3) PCT).

PATENT COOPERATION TREATY

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International filing date (day/month/year)
31.03.2005

Priority date (day/month/year)
02.04.2004

International Patent Classification (IPC) or both national classification and IPC
A61K31/424, A61P25/20, A61P11/00

Applicant
H. LUNDBECK A/S

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
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For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Bonzano, C

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

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Box No. I Basis of the opinion

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 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/DK2005/000222

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 23,24 with regard to industrial applicability

because:

- ☒ the said international application, or the said claims Nos. 23,24 with regard to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/DK2005/000222

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	7,8,20
	No: Claims	1-6,9-19,21-24
Inventive step (IS)	Yes: Claims	-
	No: Claims	1-24
Industrial applicability (IA)	Yes: Claims	1-22
	No: Claims	23,24 (see separate sheet)

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The subject matter of claims 23,24 concerns a method of treatment of the human/animal body which is considered by this Authority to be covered by the provisions of Rule 67.1 (IV) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of this claim (Article 34(4) (a)(I)PCT).

Re Item V

2. Reference is made to the following documents:

D1 : WO 00/51590 A (THE BOARD OF TRUSTEES OF THE UNIVERSITY OF ILLINOIS; RADULOVACKI, MIOD) 8 September 2000 (2000-09-08)

D2 : WO 97/02813 A (MAX-PLANCK-GESELLSCHAFT ZUR FOERDERUNG DER WISSENSCHAFT) 30 January 1997 (1997-01-30)

D3 : DUTSCHMANN M ET AL: "NMDA AND GABAA RECEPTORS IN THE RAT KOELLIKER-FUSE AREA CONTROL CARDIORESPIRATORY RESPONSES EVOKED BY TRIGEMINAL ETHMOIDAL NERVE STIMULATION" JOURNAL OF PHYSIOLOGY, vol. 510, no. 3, August 1998 (1998-08), pages 793-804, XP000922770 ISSN: 0022-3751

D4: BEULLENS J: "Sleep disorders in older people, in particular sleep apnea syndrome: Are these a cause of sleeplessness?" TIJDSCHRIFT VOOR GERONTOLOGIE EN GERIATRIE 1999 NETHERLANDS, vol. 30, no. 6, 1999, pages 256-263, XP008050219 ISSN: 0167-9228

3. For the assessment of the present claims 23,24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Novelty

4. The present application does not meet the criteria of Article 33(1) PCT, because the

subject-matter of claims 1-6,9-19,21-24 is not new in the sense of Article 33(2) PCT. Document D1 discloses a method of preventing or ameliorating sleep-related breathing disorders, in particular sleep apnea related breathing disorder, comprising administering to a patient in need thereof an effective amount of GABA receptor agonist, namely THIP (other name for gaboxadol). The subject-matter of claims 1-6,9-19,21-24 is therefore not new over D1 (Article 33(2) PCT).

Inventive step

5. The present application does not meet the criteria of Article 33(1) PCT, because the subject matter of claims 1-6,9-19,21-24, as far as novel, and 7,8,20 does not involve an inventive step in the sense of Article 33(3) PCT.

According to D4, among the most important sleep disorders is sleep apnea syndrome. The subject-matter of claims 1-24 differs from the disclosure of D4 in that sleep apnea syndrome is treated with the compound gaboxadol.

The problem to be solved by the present invention may therefore be regarded as finding an alternative treatment for sleep apnea syndrome.

Document D2 describes the GABA_A agonists muscimol and the present claimed compound THIP as having very advantageous effects on sleep: a method for treating a sleep disorder is disclosed, comprising administering a hypnotically effective amount of THIP, (other name for gaboxadol), wherein said sleep disorder is difficulty in falling asleep, frequent nocturnal arousal, wherein the amount of THIP administered is 5 to 50 mg per day.

It would be obvious for the man skilled in the art to use gaboxadol for treating sleep apnea, knowing that this compound is useful for treating sleep disorders in general and knowing that sleep apnea is one of the commonest sleep disorders.

Moreover, D3 discloses that the GABA_A antagonist bicuculline induces suppression of breathing and apnea during sleep. This teaching would strengthen the motivation of the man skilled in the art to try to use instead of a GABA_A antagonist a GABA agonist, such as gaboxadol, for treating the symptoms of apnea and stimulate breathing during sleep (Article 33(3) PCT).